44. (New) A method of developing a cell line containing a suppressor of apoptosis, comprising the steps of:

a) isolating a recombinant DNA that encodes AcNPV p35;

b) constructing a first recombinant DNA expression vector wherein said recombinant DNA is cloned into said first recombinant DNA expression vector such that said recombinant DNA is capable of being expressed in said cell line;

c) delivering said first recombinant DNA expression vector into at least one Sf9 cell;

d) exposing said at least one cell to an inducer of apoptosis; and

e) selecting said cell lines from said at least one cell which survives exposure to said inducer of apoptosis, such that apoptosis induced by a baculovirus infection is inhibited, when said baculovirus includes a functional p35 gene.

REMARKS

The Office Action of August 24, 2000 has been reviewed and its contents carefully noted. Reconsideration of this case, as amended, is earnestly requested. Claims 1-7, 9-17, 19, 26-34 and 36-44 remain in this case, claims 8, 18, 20-25 and 35 being cancelled, claims 1, 7, 10, 19, 26, 33 and 36 being amended, and new claims 37-44 being added by this response. The new claims and amendment of the claims are supported generally throughout the specification. No new matter has been added.

Rejections under 35 U.S.C. § 102

Claims 1-4, 6-7, 9-14, 16-17 and 19-25 were rejected under 35 U.S.C. 102(b) as being anticipated by Cartier *et al.* More particularly, the Examiner maintains that Cartier *et al.* teaches a stably transfected insect cell line, wherein the cells comprise a first recombinant DNA expression vector that encodes and expresses the AcNPV p35 gene, and a second recombinant DNA expression vector, which expresses a heterologous protein which can be a selectable marker and wherein the stable transfected cell line is resistant to an inducer of apoptosis.

Of the above rejected claims, only claims 1-4, 6-7, 9-14, 16-17 and 19 remain in this case, claims 20-25 being cancelled by this response.

Claim 1 is amended to overcome the rejection. More particularly, claim 1, as amended, recites an insect cell line engineered to express a suppressor of apoptosis, such that said cell line, when infected with a vector engineered to express a recombinant protein, **expresses said recombinant protein at a higher level than that of a parental cell line**, from which said cell line comprising said suppressor of apoptosis is derived. Cartier does not disclose an engineered insect cell line that expresses a recombinant protein at a higher level than that of its parental cell line. Indeed, figure 4 of Cartier indicates no significant effect on recombinant gene expression. Rather, Cartier merely discloses a cell line wherein apoptosis is inhibited when the cells are infected with a baculovirus. Thus, Cartier does not disclose each and every element of claim 1 and, therefore, the reference does not anticipate the claim. It is respectfully submitted that the rejection of claim 1 is thus overcome. Reconsideration and withdrawal of the rejection are respectfully requested.

Dependent claims 2-4, 6-7, 9-14, 16-17 and 19, being dependent upon and further limiting independent claim 1, should also be allowable for that reason, as well as for the additional recitations they contain. Reconsideration and withdrawal of the rejection of claims 1-4, 6-7, 9-14, 16-17 and 19-25 under 35 U.S.C. 102(b) are therefore respectfully requested.

Claim 15 was rejected under 35 U.S.C. 102(b) as being anticipated by Rabizadeh *et al.* Claim 15, being dependent upon and further limiting independent claim 1, should also be allowable for the reasons given above with respect to Cartier *et al.*, as well as for the additional recitations it contains. Further, Applicants' claim 15 recites an engineered insect cell line, and Rabizadeh does not disclose an insect cell line that expresses a recombinant protein at a higher level than that of its parental cell line. Rather, Rabizadeh merely discloses engineered mammalian cells. Thus, Rabizadeh does not disclose each and every element of claim 15 and, therefore, the reference does not anticipate the claim. It is respectfully submitted that the rejection of claim 15 is thus overcome. Reconsideration and withdrawal of the rejection of claim 15 under 35 U.S.C. 102(b) are therefore respectfully requested.

Claims 26, 30, 32 and 33 were rejected under 35 U.S.C. 102(b) as being anticipated by McLachlin *et al.* More particularly, the Examiner maintains that McLachlin *et al.* recites a method for developing a cell line containing a suppressor of apoptosis, comprising exposing the cell to an inducer of apoptosis (*i.e.* actinomycin-D) and selecting cells which survivc exposure to the inducer of apoptosis. Applicants respectfully disagree with the rejection.

Claim 26, as amended, recites a method of developing a cell line comprising, *inter alia*, the steps of **exposing said host cell to an inducer of apoptosis** and **selecting cells which survive exposure to said inducer of apoptosis**. Although the Examiner asserts otherwise, McLachlin actually does not disclose a method of developing a cell line comprising the steps of exposing said host cell to an inducer of apoptosis and selecting the surviving cells. Rather, McLachlin merely discloses a cell line wherein apoptosis is inhibited, when the cells are exposed to actinomycin-D. A careful reading of the McLachlin reference indicates clearly that the cells were not selected by exposing them to an inducer of apoptosis (*i.e.*, actinomycin-D). Indeed, the cells were exposed to actinomycin-D merely to show their resistance to an inducer of apoptosis; they were not exposed to actinomycin-D as part of a selection scheme, or selected after such exposure for cells that survived the treatment. Thus, McLachlin does not disclose each and every element of claim 26 and, therefore, the reference does not anticipate the claim. It is respectfully submitted that the rejection of claim 26 is thus overcome. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Dependent claims 30, 32 and 33, being dependent upon and further limiting independent claim 26, should also be allowable for that reason, as well as for the additional recitations they contain. Reconsideration and withdrawal of the rejection of claims 26, 30, 32 and 33 under 35 U.S.C. 102(b) are therefore respectfully requested.

Rejections under 35 U.S.C. § 103

Applicant acknowledges the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made, in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103 (a).

Claim 5 was rejected under 35 U.S.C. 103(a) as being unpatentable over Cartier *et al.* in view of Rabizadeh *et al.*

Claim 5, being dependent upon and further limiting independent claim 1, recites an insect cell line engineered to express a suppressor of apoptosis, such that said cell line, when infected with a vector engineered to express a recombinant protein, **expresses said recombinant protein at a higher level than that of a parental cell line**, from which said cell line comprising said suppressor of apoptosis is derived. The Cartier and Rabizadeh references, whether taken alone or in combination, do not disclose, teach or suggest an engineered insect cell line that expresses a recombinant protein at a higher level than that of its parental cell line. Further, the references, whether taken alone or in combination, do not disclose, teach or suggest such an insect line that is resistant to nutrient stress. Rather, Cartier merely discloses a cell line wherein apoptosis is inhibited when the cells are infected with a baculovirus. Rabizadeh does not cure the deficiencies of Cartier, as Rabizadeh merely discloses a mammalian cell line resistant to nutrient stress. Indeed, the differences between mammalian and insect cells are so great (*e.g.*, suitable media and sera, required nutrients, pH, culture temperature, gas requirements, etc.) that one of ordinary skill in the art would not reasonably expect teachings in regard to nutrient stress mammalian cells to apply to insect cells. Further, figure 4 of Cartier indicates no significant effect on recombinant gene expression. Thus, the prior art teaches away from the invention of claim 5. It is respectfully submitted that the obviousness rejection is thus overcome. Reconsideration and withdrawal of the rejection of claim 5 under 35 U.S.C. 103(a) are therefore respectfully requested.

Claims 8 and 18 were rejected under 35 U.S.C. 103(a) as being unpatentable over Cartier *et al.* in view of Mastrangelo *et al.*

Claims 8 and 18 are cancelled. Reconsideration and withdrawal of the rejection of claims 8 and 18 under 35 U.S.C. 103(a) are therefore respectfully requested.

Rejections under 35 U.S.C. § 112

Claims 1-2, 4-21, 23-24 and 26-36 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully disagree with the rejection.

Of the above rejected claims, only claims 1-2, 4, 6, 8-9, 13, 26-30 and 32-36 remain in this case, claims 5, 7, 10-12, 14-25 and 31 being cancelled by this response.

The Examiner maintains that the instant claims read on a genus of cell lines from any source stably transfected with any gene encoding any suppressor of apoptosis, a genus of expression vectors encoding suppressors of apoptosis from any source, and a genus of methods employing said suppressors of apoptosis and cell lines containing said genes. The Examiner further maintains that Applicants present only examples of Sf9 insect cells stably transformed with the AcNPV p35 gene, expression vectors containing this gene, and a method of developing Sf9 cell lines stably transfected with the AcNPV p35 gene. Thus, the Examiner concludes that Applicants' disclosure is insufficient to provide an adequate written description of the claimed genus of cell lines.

The present Application expressly describes several different cell lines in which the teachings of the disclosure can be applied. See Applicants' specification at page 8, lines 24-30. Further, baculoviruses, vectors and suppressors of apoptosis are all well known in the art.

The general rule on adequacy of disclosure is that disclosure of a single species is adequate support for a generic claim. In re Bowen, 181 USPQ 48, 50 (CCPA 1974). It is well established that a patent applicant is entitled to claim his invention generically, when he describes it sufficiently to meet the requirements of Section 112. *See* Utter v. Hiraga, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988) ("A specification may, within the meaning of 35 U.S.C. §112¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses."); In re Robins, 166 USPQ 552, 555 (CCPA 1970) ("[R]epresentative samples are not required by the statute and are not an end in themselves."). In In re Rasmussen the court restated the uncontroversial proposition that "a claim may be broader than the specific embodiment disclosed in a specification." 211 USPQ 323, 326 (CCPA 1981).

It is respectfully submitted that Applicants have satisfied the written disclosure requirement for the claimed genus by disclosure of the identifying characteristics and, more particularly, by expressly identifying with particularity several different cell lines in which the teachings of the disclosure can be applied. Therefore, reconsideration and withdrawal of the rejection of claims 1-2, 4-21, 23-24 and 26-36 under 35 U.S.C. 112, first paragraph are respectfully requested.

Claims 1-2, 4-21, 23-24 and 26-36 were rejected under 35 U.S.C. 112, first paragraph, as not being enabling for any cell or insect cell stably transfected with any gene encoding any suppressor of apoptosis, any DNA expression vector encoding any gene encoding any suppressor of apoptosis and a method of making any cell line stably transfected with a gene encoding a suppressor of apoptosis. Applicants respectfully disagree with the rejection.

The general rule on adequacy of disclosure is that disclosure of a single species is adequate support for a generic claim. In re Bowen, 181 USPQ 48, 50 (CCPA 1974). It is well established that a patent applicant is entitled to claim his invention generically, when he describes it sufficiently to meet the requirements of Section 112. *See* Utter v. Hiraga, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988) ("A specification may, within the meaning of 35 U.S.C. §112¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses."); In re Robins, 166 USPQ 552, 555 (CCPA 1970) ("[R]epresentative samples are not required by the statute and are not an end in themselves."). In In re Rasmussen the court restated the uncontroversial proposition that "a claim may be broader than the specific embodiment disclosed in a specification." 211 USPQ 323, 326 (CCPA 1981).

Claims 7-8, 18-19 and 35-36 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. More particularly, the Examiner maintains that claims 7, 19 and 35 are vague, in that it is unclear when the cell is infected by the baculovirus (*i.e.* before transfection with the gene encoding the suppressor of apoptosis, or after transfection).

Claims 7, 19 and 35 are amended to overcome the rejection. More particularly, the claims are amended to expressly recite a cell line containing a suppressor of apoptosis that is infected by a baculovirus. Thus, it is clear from the language of the amended claims that the cell

is infected by the baculovirus after transfection with a gene encoding a suppressor of apoptosis. It is respectfully submitted that the rejection is thus overcome, and that there are no other ambiguities in the claims. Reconsideration and withdrawal of the rejection of claims 7, 19 and 35 as being indefinite under 35 U.S.C. 112, second paragraph, are respectfully requested.

The Examiner further maintains that claims 8, 18 and 35 are vague in the recitation of a cell line capable of expressing a recombinant protein at a higher level than that from a parental cell line from which said cell line is derived, because the Examiner asserts that it is unclear when the cell line is capable of expressing the protein at higher levels and when it is not capable of expressing the protein at higher levels.

Claims 8, 18 and 35 are cancelled by this response. Reconsideration and withdrawal of the rejection of claims 8, 18 and 35 as being indefinite under 35 U.S.C. 112, second paragraph, are respectfully requested.

In addition, the Examiner's attention is drawn to the fact that the present Amendment merges the limitations of claims 8, 18 and 35 into claims 1, 10 and 26, respectively. Thus, in regard to the indefiniteness rejection, the language which the Examiner apparently finds confusing is amended to expressly recite a cell line that expresses a recombinant protein at a higher level than that of a parental cell line. It is respectfully submitted that there are no ambiguities in the claims.

Conclusion

Applicant believes the claims, as amended, are patentable over the prior art, and that this case is now in condition for allowance of all claims therein. Such action is thus respectfully requested. If the Examiner disagrees, or believes for any other reason that direct contact with Applicants' attorney would advance the prosecution of the case to finality, he is invited to telephone the undersigned at the number given below.

"Recognizing that Internet communications are not secured, I hereby authorize the PTO to communicate with me concerning any subject matter of this application by electronic mail. I understand that a copy of these communications will be made of record in the application file."

Respectfully Submitted:
—Blissard et al--

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